Public Health and Preventive Medicine

Rabies Preexposure Prophylaxis

JONATHAN MANN, MD, MPH, *and* MICHAEL J. BURKHART, MPH, *Santa Fe, New Mexico*

One of a series of articles from western state public health departments

Rabies preexposure prophylaxis, protection for persons at "high risk" of future exposures to rabies virus, has generally received less attention than postexposure prophylaxis, the protection of persons after exposure to rabid or potentially rabid animals. Recent developments in rabies vaccine testing and technology for preexposure prophylaxis justify new interest from both public health and private practitioner viewpoints.

Preexposure prophylaxis with rabies vaccines became feasible and reasonable following development of rabies vaccines with a sufficiently low risk of serious side effects to warrant their preexposure use.[1] Preexposure prophylaxis has three potentially attractive features.[2] First, preexposure prophylaxis may protect the recipient against inapparent exposures to rabies virus—as could happen when the diagnosis of rabies is not considered in an animal biting a veterinarian or when an accident occurs in a laboratory handling live rabies virus. Second, if a victim's ability to obtain prompt postexposure prophylaxis is impaired, as might occur on an expedition in remote areas or to a missionary or health worker in third-world countries, preexposure prophylaxis may provide a level of protection against rabies while awaiting the start of postexposure prophylaxis. Third, since a preexposure prophylaxis recipient develops an anamnestic serologic response to subsequent rabies vaccine injections, the recipient's postexposure prophylactic regimen is cheaper and simpler than for those who have not received preexposure prophylaxis. Specifically, postexposure prophylaxis for preexposure prophylaxis recipients requires only two separate intramuscular injections of rabies vaccine three days apart, compared with the standard postexposure prophylactic course of five intramuscular vaccine injections over a 28-day period plus a single injection of rabies antiserum.[2] At current prices for human diploid cell vaccine (HDCV) and human rabies immune globulin (RIG) for a 70-kg person, the cost differential between these two postexposure regimens is approximately $335 (at a cost of $42.50 per HDVC dose, $160 for RIG and $15 per medical visit). Additional arguments favoring preexposure prophylaxis include the extreme rarity of rabies among preexposure prophylaxis recipients known to have responded serologically to rabies vaccine[3] and the safety of HDCV compared with all previously available rabies vaccines.[4] Reactions to HDCV are generally mild, with approximately 25% of recipients reporting local reactions and 20% experiencing systemic reactions such as headache, nausea or myalgia.[2] Allergic reactions are rare. Two cases of transient neuroparalytic illness among more than 330,000 HDCV recipients worldwide have been reported.[5]

The important new work in preexposure prophylaxis involves an intradermal regimen using HDCV.[6,7] As recently summarized by the Centers for Disease Control, all of more than 1,500 people lacking rabies antibody who received three 0.1 ml doses of HDCV intradermally (one dose each on days 0, 7 and 21 or 28) developed adequate antibody titers.[8] The intradermal injections are given in the skin overlying the deltoid to increase the probability of actual intradermal delivery; however, inadvertent subcutaneous administration also appears effective in inducing antibody production.[7] The high immunogenicity of HDCV virtually guarantees seroconversion in immunologically normal persons. Therefore, with the exception of persons known to be immunocompromised and workers in rabies vaccine production or rabies research, serologic testing to document a "take" of HDCV following preexposure prophylaxis is not recommended.[9] Finally, by the end of 1983 one of the two manufacturers of rabies vaccine licensed for use in the United States (Merieux Institute) plans to market HDCV in a special package for intradermal use only, at an estimated per dose cost of $15. Pending release of this package, currently avail-

Refer to: Mann J, Burkhart MJ: Rabies preexposure prophylaxis (Public Health and Preventive Medicine). West J Med 1983 Sep; 139:386-387.

Dr Mann is State Epidemiologist, New Mexico Health and Environment Department, and Mr Burkhart is Director, Health Services Division, New Mexico Health and Environment Department, Santa Fe.

Reprint requests to Jonathan Mann, MD, MPH, New Mexico Health and Environment Department, PO Box 968, Santa Fe, NM 87503.

ABBREVIATIONS USED IN TEXT

HDCV=human diploid cell rabies vaccine
RIG=(human) rabies immune globulin

able 1-ml HDCV vials may be used for intradermal vaccine administration, but the vials are not intended for multidose use.

Candidates for preexposure prophylaxis include persons whose vocation, avocation or special circumstances place them at higher than average risk for exposure to rabies and particularly to risk of inapparent or unnoticed exposure to the virus. Veterinarians; veterinary assistants; animal control officers; trappers, spelunkers; biologists working with animal hosts of rabies virus (bats, skunks, raccoons, foxes and other species at high risk); laboratory workers in rabies diagnostic, veterinary, rabies vaccine and rabies research laboratories; travelers to certain rabies-enzootic areas (particularly where dog rabies is enzootic), and missionaries or health workers residing in rabies-enzootic areas can all be considered for preexposure prophylaxis.[1,2,7] While the proportion of candidates who actually receive preexposure prophylaxis is unknown, our experience in New Mexico suggests that few veterinary assistants, trappers or naturalists and only a minority of animal control workers have been vaccinated. In addition, while most veterinary students in the past five years have received preexposure prophylaxis in veterinary school, older veterinarians may lack adequate preexposure prophylaxis.

If preexposure prophylaxis is to be given, the recipient must understand that it cannot be relied upon for protection against rabies. Rather, if exposed to a rabid or potentially rabid animal, a limited postexposure prophylactic regimen (described above) will be necessary. Finally, if ongoing preexposure prophylaxis is desired, the Centers for Disease Control recommend that a single 0.1 ml intradermal booster dose of HDCV be administered every two years (exceptions are rabies vaccine and research workers who require closer monitoring and may need periodic titer checks and more frequent boosters).[2,8]

Now that preexposure prophylaxis is extremely safe and the vaccine cost will be greatly reduced, public health officials should consider strategies to increase preexposure prophylaxis coverage of selected high-risk groups. Physicians should welcome the advent of intradermal HDCV use, systematically question patients about their possible need for preexposure prophylaxis and consult with local and state health departments if questions arise regarding indications, details of administration and side effects of HDCV.

REFERENCES

1. Tierkel ES, Sikes RK: Preexposure prophylaxis against rabies: Comparison of regimens. JAMA 1967 Sep; 201:911-914

2. Rabies prevention. Morbidity Mortality Weekly Rep 1980 Jun 13; 29:265-280

3. Rabies in a laboratory worker—New York. Morbidity Mortality Weekly Rep 1977 Jun 3; 26:183-184

4. Dales L: Side effects of human diploid cell rabies vaccine and human rabies immune globulin. West J Med 1982 Jan; 136:48-49

5. Bernard KW, Smith PW, Kader FJ, et al: Neuroparalytic illness and human diploid cell rabies vaccine. JAMA 1982 Dec; 248:3136-3138

6. Ajjan N, Soulebot JP, Triau R, et al: Intradermal immunization with rabies vaccine: Inactivated Wistar strain cultivated in human diploid cells. JAMA 1980 Dec 5; 244:2528-2531

7. Bernard KW, Roberts MA, Sumner J, et al: Human diploid cell rabies vaccine: Effectiveness of immunization with small intradermal or subcutaneous doses. JAMA 1982 Feb 26; 247:1138-1142

8. Supplementary statement on pre-exposure rabies prophylaxis by the intradermal route. Morbidity Mortality Weekly Rep 1982 Jun 4; 31: 279-280, 285

9. Supplementary statement on rabies vaccine and serologic testing. Morbidity Mortality Weekly Rep 1981 Oct 30; 30:535-536